Isolated Left Ventricular Noncompaction in Sub-Saharan Africa: A Clinical and Echocardiographic Perspective

Ferande Peters, MD; Bijoy K. Khandheria, MD; Claudia dos Santos, BSc; Hiral Matioida, BSc; Nirvarthi Maharaj, MD; Elena Libhaber, PhD; Farouk Mamdoo, MD; Mohammed R. Essop, MD

Background—Isolated left ventricular noncompaction (ILVNC) is a cardiomyopathy caused by intrauterine failure of the myocardium to compact. Common clinical complications are heart failure, arrhythmias, and cardioembolism. A paucity of data exists relating to clinical and echocardiographic features of ILVNC in Africans.

Methods and Results—This study is a single-center, prospective case-control study, whereby subjects attending a dedicated cardiomyopathy clinic were screened for and diagnosed with ILVNC, provided they had no other associated structural heart disease and fulfilled all the accompanying echocardiographic criteria: (1) end-systolic ratio of noncompacted layer to compacted layer >2, (2) presence of >3 prominent apical trabeculations, and (3) deep intertrabecular recesses that fill with blood from the ventricular cavity visualized using color Doppler ultrasound. Fifty-four subjects were identified, age 45.4±13.1 years (mean±SD), 95% confidence interval 3.6 to 10.2, 55.6% male, and 63.0% New York Health Association Class II, and prevalence of LVNC in our clinic was 6.9%, 95% confidence interval 3.6 to 10.2. Heart failure because of systolic dysfunction was the most common clinical presentation (53 subjects, 98.1%). Left ventricular end-diastolic diameter was 61.4±7.2 mm (mean±SD) and ejection fraction 26.7±11.9% (mean±SD). Common sites of noncompaction were the apical (100%), midinferior (74.1%), and midlateral (64.8%) walls. Right ventricular noncompaction occurred in 12 subjects (22.2%). Pulmonary hypertension was documented in 45 cases (83.3%). Right ventricular dilation was noted in 40 subjects (74.1%), while right ventricular function was depressed in 32 (59.3%). Tricuspid S' was 9.6±2.8 cm/s (mean±SD). No echocardiographic features suggestive of ILVNC were noted in a healthy control group of African descent.

Conclusions—ILVNC in patients of African descent can be characterized by biventricular abnormality and pulmonary hypertension, in addition to isolated left-sided abnormality. (Circ Cardiovasc Imaging. 2012;5:187-193.)

Key Words: isolated left ventricular noncompaction ■ Africa ■ cardiomyopathy

Isolated left ventricular noncompaction (ILVNC) is a cardiomyopathy caused by intrauterine failure of the myocardium to compact. This malformation occurs in the absence of any coexisting congenital heart defects and was first described by Chin et al in 1990. It is a rare disorder with a reported prevalence between 0.05% and 0.25%. During the last 10 years, increasing awareness of this condition, accompanied by improved diagnostic imaging techniques, have resulted in the recognition of more ILVNC cases worldwide, which allowed the clinical characteristics to be better defined. Heart failure, thromboembolism, and malignant ventricular arrhythmias are the most challenging clinical aspects of ILVNC confronting clinicians worldwide, and have contributed to the poor survival observed in these patients. In sub-Saharan Africa, the most common causes of heart failure are thought to be related to rheumatic valvular disease, peripartum and idiopathic cardiomyopathy, and hypertension. In the Heart of Soweto Study, the largest prospective modern study of heart failure in Africa that used clinical and echocardiographic assessment, 28% of all heart failure was caused by idiopathic cardiomyopathy. A Medline (ProQuest LLC) search revealed that only sporadic case reports of ILVNC could be identified in patients from Africa. We prospectively documented the clinical and echocardiographic features of patients identified with ILVNC and compared them with a group of healthy controls.

Methods

We conducted a single-center, prospective case-control study. From July 2009 to December 2010, 780 patients of African ancestry were referred to the Chris Hani Baragwanath Hospital cardiomyopathy clinic with a presumed diagnosis of dilated cardiomyopathy. The Baragwanath dilated cardiomyopathy registry was established in June 2009 after receiving approval from the University of the Witwatersrand Ethics Committee. The purpose of this registry is to

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valvular regurgitation. In cases of eccentric regurgitation, or where (TR) were analyzed in accordance with the ASE guidelines on native chamber quantification guidelines of 2006. All right performed in accordance with the American Society of Echocardiography (ASE) and analyzed offline.

All data were transferred to an Xcelera workstation (Philips Healthcare) equipped with an S5-1 transducer (frequency transmitted 1.7 MHz, received 3.4 MHz), according to a standardized protocol. Comprehensive transthoracic echocardiography was performed using a commercially available system (iE33 xMATRIX, Philips Healthcare) equipped with an S5-1 transducer (frequency transmitted 1.7 MHz, received 3.4 MHz), according to a standardized protocol. All data were transferred to an Xcelera workstation (Philips Healthcare) and analyzed offline.

Measurements relating to left heart size and function were performed in accordance with the American Society of Echocardiography (ASE) chamber quantification guidelines of 2006. All right heart parameters were performed and compared with normal reference values defined in the ASE 2010 guidelines on right heart assessment. The severity of mitral (MR) and tricuspid regurgitation (TR) were analyzed in accordance with the ASE guidelines on native valvular regurgitation. In cases of eccentric regurgitation, or where severe regurgitation could not be excluded, quantification was performed to distinguish moderate from severe valvular regurgitation.

Isolated Left Ventricular Noncompaction

All echocardiograms were analyzed by a single cardiologist (F.P.). Provided there was no evidence of congenital or acquired heart disease, only subjects definitely satisfying all the criteria were diagnosed as having ILVNC. The criteria proposed by Oeschlin, Jenni, and colleagues were modified by requiring that the trabeculated portions of the left ventricle satisfy criteria that would less likely be found in normal individuals: (1) the ratio of the noncompacted endocardial layer compared with the compacted epicardial layer had to be >2 measured at end systole (Figure 1A), (2) presence of more than 3 prominent trabeculations in the left ventricular (LV) apex that did not originate from the septum, and (3) deep intertrabecular recesses that filled with blood from the ventricular cavity as visualized on color Doppler ultrasound (Figure 1B, 1C).

The location of noncompaction was described using a 9-segment model proposed by Jenni et al in one of the largest series described. The apex was defined as caudal to the papillary muscles, while the base was defined as the area of the left ventricle cranial to the tips of the mitral valve, with the midsegment being the area between these 2 segments. The whole apex was regarded as 1 segment, while the base and midsegment were divided into 4 segments each (inferior, lateral, anterior, and septal).

Right Ventricular Noncompaction

While right ventricular (RV) noncompaction has been described in autopsy studies, its occurrence in clinical scenarios is limited to isolated case reports. Concomitant RV noncompaction was diagnosed in our series only in cases where a bilayered structure with flow within the trabeculae could be noted in the basal and midfree wall of the right ventricle, and if these areas had no bands extending onto the septum (Figure 2).

Statistical Methods

Descriptive statistics are presented as means±standard deviation for continuous variables, or frequencies and percentages for categorical variables. Comparisons between the ILVNC group and controls were evaluated using analysis of covariance (ANCOVA) techniques, with age and gender as covariates and performed to distinguish moderate from severe valvular regurgitation.

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Statistical significance was defined as 2-tailed \( P<0.05 \). Statistical analyses were performed using a SAS 9.12 statistical program (SAS Institute Inc.).

### Results

A total of 54 patients with ILVNC were identified; their baseline characteristics are depicted in Table 1. The prevalence of ILVNC in our cardiomyopathy clinic was 6.9% (95% confidence interval 3.6–10.2). Mean age of this cohort was 45.4 years, and 55.6% were male. All but 1 patient had documented heart failure. At enrollment, most patients were on standard systolic heart failure therapy (98.1%), and the majority was New York Heart Association Class II (63.0%). One subject was diagnosed with ILVNC with a normal EF after being referred for an echocardiogram as part of the evaluation for chest discomfort. In 1 subject, a ventricular tachycardia storm occurred that was successfully treated with subsequent implantation of an implantable cardioverter-defibrillator. Cardioembolism was documented in 1 subject, with no evidence of LV thrombus on echocardiography. No cases of facial dysmorphism or neuromuscular abnormality were noted in this series.

#### Echocardiography

Mean left ventricular end-diastolic diameter of the cohort was 61.4 mm, and the mean left ventricular ejection fraction was 26.7%, with severe global LV dysfunction (EF <30%) occurring in two-thirds of patients, all of which differed considerably to the control group (\( P<0.0001 \)). Within the LV cavity, spontaneous echo contrast was noted in one-third of patients, while thrombi were documented in 5 patients (9.3%). A significant degree of MR was noted in two-thirds of subjects (moderate MR: 42.6%, severe MR: 24.1%). Restrictive hemodynamics with mitral inflow Doppler analysis at baseline were noted in 20.5% of patients, all of whom had a subnormal EF (Table 2).

#### Isolated Left Ventricular Noncompaction

All 9 segments were evaluated successfully in all patients diagnosed with ILVNC. The LV apex was most commonly the site of noncompaction, and the base of the heart was the least involved. Using the 9-segment model, midinferior and midlateral walls were the next most common segments in which noncompaction could be found (Table 3). Mean ratios of the noncompacted/compacted myocardium in all 5 regions where noncompaction was found are depicted in Figure 3. The base was very infrequently involved and, when it occurred, the noncompaction was found only in the inferior and lateral walls. All involved segments were equally hypokinetic compared with surrounding myocardium, except in

### Table 1. Clinical Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of ILVNC</th>
<th>Control</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>(n=54)</td>
<td>(n=54)</td>
</tr>
<tr>
<td>Age (y)*</td>
<td>45.4±13.1</td>
<td>38.9±10.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Male sex, no. (%)</td>
<td>30 (55.6%)</td>
<td>28 (51.9%)</td>
<td>0.85</td>
</tr>
<tr>
<td>Documented heart failure, no. (%)</td>
<td>53 (98.1%)</td>
<td>...</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NYHA class on therapy, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>12 (22.2%)</td>
<td>54 (100%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>34 (63.0%)</td>
<td>...</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>III</td>
<td>8 (14.8%)</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg*</td>
<td>111.2±19.5</td>
<td>126.3±12.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg*</td>
<td>73.1±12.3</td>
<td>77.5±10.7</td>
<td>0.11</td>
</tr>
</tbody>
</table>

ILVNC indicates isolated left ventricular noncompaction; NYHA, New York Heart Association.

*Mean ± standard deviation.

### Table 2. Left Heart Echocardiographic Features

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. of ILVNC</th>
<th>Control</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>(n=54)</td>
<td>(n=54)</td>
</tr>
<tr>
<td>LVEDD, mm*</td>
<td>61.4±7.2</td>
<td>43.9±4.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVWT, mm*</td>
<td>8.4±1.8</td>
<td>10.1±2.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVPWd, mm*</td>
<td>9.4±2.2</td>
<td>9.0±1.7</td>
<td>0.6</td>
</tr>
<tr>
<td>LV EF, %</td>
<td>25.9±11.6</td>
<td>61.15±6.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LA volume, mL*</td>
<td>78.2±34.2</td>
<td>34.3±14.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV thrombus, no. (%)</td>
<td>5 (9.3%)</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>LV SPEC, no. (%)</td>
<td>18 (33.3%)</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>MR, total no. (%)</td>
<td>49 (90.7%)</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Mild, no. (%)</td>
<td>13 (24.1%)</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Moderate, no. (%)</td>
<td>23 (42.6%)</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Severe, no. (%)</td>
<td>13 (24.1%)</td>
<td>...</td>
<td></td>
</tr>
</tbody>
</table>

ILVNC indicates isolated left ventricular noncompaction; LVEDD, left ventricular end-diastolic diameter; LVWT, interventricular septal thickness at diastole; LVPWd, left ventricular posterior wall thickness at diastole; LV EF, left ventricular ejection fraction; LA, left atrium; LV, left ventricular; SPEC, spontaneous echo contrast; MR, mitral regurgitation.

*Mean ± standard deviation.
the isolated case in which the patient had a normal EF and no regional wall abnormality was detected.

No subjects in the control group satisfied the diagnostic criteria for ILVNC proposed in this study, which required that all the proposed criteria be present. All 9 segments (as proposed by Jenni et al4 for evaluation of ILVNC) were successfully evaluated in all subjects in the control group. A trabeculated apex was noted in 20 subjects (37.0%), with 5 subjects (9.3%) having more than 4 trabeculations noted in the apical area. While 3 subjects (5.6%) had a bilayered appearance to the myocardium in the trabeculated area, the end-systolic ratio was not >2 in any of the controls (mean end-systolic ratio for the 3 controls was 1.16±0.27).

Papillary Muscle Abnormality
A distinct abnormality of papillary muscle architecture was noted in 26 patients (48.1%). The papillary muscle was absent or rudimentary in 36 cases and involved the posteromedial papillary muscle in 16 (29.6%) and the anterolateral papillary muscle in 20 (37%). In all cases, absence of the papillary muscle or the presence of a rudimentary papillary muscle occurred where the midsegment of the left ventricle displayed features of extensive noncompaction involving either the inferior or lateral walls or both. All subjects in the control group had well-formed papillary muscles with normal adjacent myocardial walls.

Right Heart Abnormality in Isolated Left Ventricular Noncompaction
Right ventricular noncompaction was noted in 12 subjects (22.2%). Pulmonary pressures were elevated in 45 of the subjects with ILVNC (83.3%), with a mean systolic pulmo-

![Figure 3](image-url)

**Figure 3.** Distribution of left ventricular segments affected by noncompaction and their ratios of noncompacted to compacted myocardium.

<table>
<thead>
<tr>
<th>Site</th>
<th>n=54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apex, no. (%)</td>
<td>54 (100%)</td>
</tr>
<tr>
<td>Midinferior, no. (%)</td>
<td>40 (74.1%)</td>
</tr>
<tr>
<td>Midlateral, no. (%)</td>
<td>35 (64.8%)</td>
</tr>
<tr>
<td>Basal inferior, no. (%)</td>
<td>9 (16.7%)</td>
</tr>
<tr>
<td>Midanterior, no. (%)</td>
<td>4 (7.4%)</td>
</tr>
</tbody>
</table>

*No other sites were involved other than those depicted here.

Table 3. Common Sites of Isolated Left Ventricular Noncompaction

Table 4. Right Heart Echocardiographic Measurements

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ILVNC (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right ventricular dilation, total no. (%)</td>
<td>40 (74.1%)</td>
</tr>
<tr>
<td>Mild, no. (%)</td>
<td>12 (22.2%)</td>
</tr>
<tr>
<td>Moderate, no. (%)</td>
<td>6 (11.1%)</td>
</tr>
<tr>
<td>Severe, no. (%)</td>
<td>22 (40.7%)</td>
</tr>
<tr>
<td>Tricuspid regurgitation, total no. (%)</td>
<td>51 (94.4%)</td>
</tr>
<tr>
<td>Mild, no. (%)</td>
<td>22 (40.7%)</td>
</tr>
<tr>
<td>Moderate, no. (%)</td>
<td>16 (29.6%)</td>
</tr>
<tr>
<td>Severe, no. (%)</td>
<td>13 (24.1%)</td>
</tr>
<tr>
<td>Systolic pulmonary artery pressure, mm Hg*</td>
<td>45.8±17.4</td>
</tr>
<tr>
<td>Tricuspid S', cm/s*</td>
<td>9.6±2.8</td>
</tr>
</tbody>
</table>

ILVNC indicates isolated left ventricular noncompaction; S', peak systolic annular tissue velocity.

*Mean ± standard deviation.

nary artery pressure of 45.5 mm Hg (Table 4). Tricuspid regurgitation was documented in 51 patients (94.4%), with severe TR in 24.1% and moderate TR in 29.6%. The right ventricle was dilated in 74.1% of cases, with severe RV dilatation occurring in 40.7% of subjects. The tricuspid peak systolic annular tissue velocity (S') was measured successfully at the lateral tricuspid annulus in 52 cases (96.3%) and was reduced in 32 (59.3%) cases, with a mean tricuspid S' of 9.6 cm/s for the entire cohort. Four cases had no right heart abnormality documented (normal pulmonary pressures, normal RV function, no RV noncompaction, and no TR). These findings differed markedly from the control group in which no RV dilatation, pathological TR, or pulmonary hypertension was detected. The mean tricuspid S' was 12.3 cm/s for the control group. The proposed criteria for RV noncompaction were not detected in any of the controls.

Discussion
Isolated left ventricular noncompaction has been classified as a specific cardiomyopathy in recent guidelines. Recognition of this condition is important because these patients have significant mortality and morbidity related to severe heart failure and malignant ventricular arrhythmias. This large prospective study of subjects of African ancestry is the first to document the unique clinical challenges in the diagnosis of patients with ILVNC in sub-Saharan Africa. Heart failure was the predominant manifestation of ILVNC in this study and, as expected, was accompanied by significant remodeling and dysfunction of the left ventricle in all but 1 instance. This study is significant in that it also highlights the significant prevalence of concomitant right heart abnormality in this population.

The time to clinical presentation of the ILVNC phenotype is highly variable; the mean age at diagnosis of this cohort was 45.8 years. This may not truly reflect the actual age at which the disease manifested because many patients were treated for dilated cardiomyopathy with systolic heart failure prior to being referred to our clinic, where diagnosis of ILVNC was made for the first time. Similar to other studies, severe LV dilatation and dysfunction accompanied by heart failure were the major clinical manifestations in our
study population. The prevalence of heart failure was much greater in this cohort compared with other series,\textsuperscript{4,15–17} because patients were most likely diagnosed later in their disease course and gained access to tertiary cardiac care much later than in other centers because of the resource-deprived environment in which we practice. The low prevalence of cardioembolism and significant arrhythmias compared with other published series\textsuperscript{4,16} is most likely a reflection of the shorter period of follow-up in our study.

Similar to other series,\textsuperscript{4,15} the predominant location of noncompaction in the left ventricle was in the apex and midinferior and midlateral walls. A unique observation in this series not well documented by others is that the papillary muscle architecture on echocardiography was either distorted or absent (Figure 4) in almost half of the patients (48.1\%) studied. The association of ILVNC with abnormality of papillary muscle architecture only has been documented previously in a Polish case report.\textsuperscript{18} In an autopsy study, Burke et al\textsuperscript{10} found that in all of their cases of ILVNC there were poorly formed papillary muscles of the left ventricle. This observation needs to be evaluated in other populations, and may have additional clinical significance with respect to the mechanism of significant MR, which was documented in two-thirds of our patients.

Both under- and overdiagnosis of ILVNC represent a major clinical challenge. In this series, no patient was diagnosed prior to assessment in our clinic despite many patients having had echocardiography performed elsewhere. This highlights the need for a high clinical index of suspicion to correctly identify the disease. Any patient with clinical features suggestive of dilated cardiomyopathy should be referred for echocardiography. This echocardiogram must be obtained systematically with careful regional wall analysis to correctly and accurately evaluate the apex on short axis to exclude ILVNC. In addition, heart failure in a setting such as ours is frequently accompanied by comorbid conditions such as HIV, malnutrition, and alcoholism, which make accurate diagnosis of ILVNC more difficult. We excluded patients with any associated illness or factors that may have contributed to LV dysfunction, particularly HIV, which has a very high prevalence in our setting. Therefore, we have underestimated the true burden of ILVNC.

Differentiating a normally trabeculated left ventricle from less overt ILVNC can be difficult. This difficulty assumes greater significance in black patients in whom phenotypic expression of LV hypertrophy and trabeculation may differ qualitatively and quantitatively compared with white patients. In a recent study, 8.3\% of normal controls fulfilled criteria for the diagnosis of ILVNC.\textsuperscript{20} The authors also noted a higher incidence of trabeculation patterns fulfilling current diagnostic criteria for ILVNC in black patients irrespective of the presence of LV disease.\textsuperscript{20} As of this time, it is unclear whether diagnostic criteria for ILVNC need to be modified depending on race. In this study, we used the presence of more than 3 trabeculae in the LV apex as a major criterion to identify patients who may have ILVNC. The rationale for this was based on a pathoanatomic study that found more than 3 trabeculations were present in only 4\% of individuals.\textsuperscript{21} Furthermore, by requiring that all the inclusion criteria for ILVNC be satisfied for diagnosis, as opposed to merely considering the degree of trabeculation in isolation as the sole criterion, we believe that we avoided the problem of overdiagnosis. The prevalence of ILVNC in our clinic was 6.9\% from a cohort of 780 subjects screened, which is based on applying comprehensive echocardiographic criteria and not merely the presence of hypertrabeculation, as in other studies. Thus, we have decreased the likelihood of overdiagnosis of ILVNC by omitting some of the 727 subjects who may have fulfilled some but not all the criteria.

A major finding in this study is the frequency of right heart abnormality, which to our knowledge has not been reported in any large series of patients with ILVNC. A report of biventricular noncompaction associated with significant pulmonary hypertension was documented in 2009.\textsuperscript{22} The evaluation of RV function is challenging in this cohort because the presence of trabeculation makes echocardiographic measurements that are dependent on endocardial border detection, such as fractional area change, difficult. Using the tricuspid S’ derived from pulsed-wave tissue Doppler of the lateral tricuspid annulus as a marker of RV longitudinal function is technically less demanding and identified in a considerable proportion of patients with RV dysfunction (61\%). The frequent presence of coexisting pulmonary hypertension and severe TR makes it difficult to know whether the observed RV dysfunction is related primarily to left-sided heart disease, causing pulmonary hypertension, or if there is an intrinsic RV abnormality. From our observation, it would appear that much of the right-sided remodeling and dysfunction is related to pulmonary hypertension.

Right ventricular noncompaction is not well defined, with some suggesting that the criteria should be the same as those for ILVNC,\textsuperscript{23,24} and others taking a contradictory view.\textsuperscript{4} One of the problems with the diagnosis of RV noncompaction is that the apex is normally trabeculated, with bands running...
from the septum to the apex. In addition, volume or pressure overload of the right ventricle can lead to a generalized enlargement of these trabeculated areas. It is for this reason we concluded that the presence of a bilayered myocardial segment in the basal and mid-RV free wall was suggestive of noncompaction, irrespective of concomitant volume or pressure overload, if this was accompanied by flow within the noncompacted endocardial area and did not have any connections to the septum. However, this needs further evaluation with magnetic resonance imaging or autopsy specimen analysis.

This study has some important limitations. Firstly, we cannot comment on the true incidence or prevalence of ILVNC because the cohort was derived from a referred population. Secondly, given the previously well-documented observations of differences in LV geometry between blacks and whites, we cannot be certain that the diagnostic criteria for ILVNC are equally applicable in different population groups. Thirdly, because this was a referred population, it is possible that we have only described the phenotype of patients with advanced disease, especially because all the patients were referred for further evaluation of heart failure. Importantly, further larger studies to evaluate trabecular patterns in normal black patients and those with hypertension and idiopathic dilated cardiomyopathy would lay a useful foundation for the interpretation of future research and may further refine our ability to diagnose ILVNC. An additional limitation to this study is that selection of the control group was not based on exact age-matching.

While the most common clinical presentation of subjects with ILVNC in this study was heart failure, causation of heart failure cannot be concluded in this cross-sectional study. In addition to systolic heart failure, these patients have significant pulmonary hypertension and right heart abnormality, which needs further elucidation. Thus, this cohort requires long-term follow-up to define these aspects, as well as to identify the true prevalence of complications related to ILVNC. The need for device therapy, such as biventricular pacing and implantable cardioverter-defibrillator, or lifelong anticoagulation to address these complications will be a major socioeconomic challenge within our environment and will have to be carefully balanced against the needs of the deserving individual. We have not addressed the issue of familial involvement and genetic analysis, which would be an important future research and highly relevant clinical consideration.

Conclusions
Isolated left ventricular noncompaction in patients of African descent is underreported in the current literature and characterized by biventricular abnormality and pulmonary hypertension. Careful echocardiographic analysis is required to identify this condition. Long-term follow-up is essential to determine if patients of African descent have the same degree of morbidity and mortality as other populations.

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Disclosures
None.

References
9. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spence KT, Sutton MS, Stewart WJ; Chamber Quantification Writing Group; American Society of Echocardiography’s Guidelines and Standards Committee; European Association of Echocardiography; Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18:1440–1463.

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**CLINICAL PERSPECTIVE**

During the past 10 years, increasing awareness of isolated left ventricular noncompaction (ILVNC), accompanied by improved diagnostic imaging techniques, have resulted in the recognition of more ILVNC cases worldwide, which allowed the clinical characteristics to be better defined. Heart failure, thromboembolism, and malignant ventricular arrhythmias are the most challenging clinical aspects of ILVNC confronting clinicians worldwide, and have contributed to the poor survival observed in these patients. In sub-Saharan Africa, the most common causes of heart failure are thought to be related to rheumatic valvular disease, peripartum and idiopathic cardiomyopathy, and hypertension. However, a large prospective modern study of heart failure in Africa that used clinical and echocardiographic assessment found 28% of all heart failure was caused by idiopathic cardiomyopathy. We prospectively documented the clinical and echocardiographic features of patients identified with ILVNC at our institution. ILVNC in patients of African descent is characterized by biventricular abnormality and pulmonary hypertension. Careful echocardiographic analysis is required to identify this condition. Long-term follow-up is essential to determine if patients of African descent have the same degree of morbidity and mortality as other populations.
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